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Description of polyphosphazenes and their relationship to: bioerodible systems; radiation-crosslinking to give hydrogels; surface hydrogel grafting; membranes, blends, and IPN's; gel-immobilized enzymes; and ion-crosslinked hydrogels;

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Water-Soluble Polyphosphazenes and their Hydrogels

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WATER-SOLUBLE POLYPHOSPHAZENES AND THEIR HYDROGELS

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Much has been written about the special characteristics of different polymer backbone systems. Nevertheless, in spite of these differences, the side groups have a greater influence on the ambient temperature properties than does the backbone, irrespective of the type of backbone that is present. Thus, the development of methods for the incorporation of different side groups into polymers is a key step in the generation of specific combinations of properties. Two general methods exist for bringing about variations in polymer side groups: (1) The polymerization of different monomers that bear different side groups, and (2) macromolecular substitution reactions in which side groups already attached to a polymer are replaced by other units. The first method is more widely used than the second, mainly because organic macromolecular side group reactions are often relatively inefficient.

Polyphosphazenes are unusual polymers in many ways.[1-3] But their most significant advantage is the ease with which specific side groups can be linked to the phosphorus-nitrogen backbone by highly efficient substitutive techniques. Thus, by using the synthesis manifold shown in Scheme I, it is possible to vary the side group structure over a wide range. Note also that sequential or simultaneous cosubstitution can yield polymers with two or more different types of side groups per chain. This approach also allows the incorporation of side groups that generate water-solubility, hydrogel formation, or hydrophilic surface character. This talk will illustrate these principles at work.

Chart 1 gives the structures of six poly-phosphazenes that are soluble in water. Species **2** is

mainly soluble in alkaline aqueous media, provided the cations are monovalent.

Bioerodible Systems

Two of the polymers shown in Chart 1 are hydrolytically-sensitive. These are polymers **3** and **4**.[4-6] Hydrolysis leads to the formation of phosphate, ammonia, and glucose or glycerol--all bio-acceptable products. Thus, the glucosyl and glyceryl side groups are potentially important substituents or cosubstituents in bioerodible and bio-acceptible polyphosphazenes for use in controlled drug delivery, and bioabsorbable structural polymers. The glyceryl derivatives hydrolyze faster than their glucosyl counterparts.

Radiation-Crosslinking to Give Hydrogels

Polymer **1** and especially polymer **5** possess side groups that contain aliphatic carbon hydrogen bonds that are sensitive to gamma-ray induced homolytic C-H bond cleavage and free radical cross-combination to generate cross-links.[7-12] The materials formed absorb water to form hydrogels, with the cross-link density and degree of water imbibition being controllable by the radiation dose. Ultraviolet irradiation also induces the crosslinking of **5**.

Surface Hydrogel Grafting

The high sensitivity of polymer **5** to gamma-ray or ultraviolet cross-linking allows films of this polymer to be radiation-grafted to the surface of polymers that themselves bear C-H or C-Cl bonds.[13] Subsequent exposure to water creates a hydrogel layer covalently bonded to the surface of the substrate polymer. Systems based on this structure show anti-microbial activity, a property that may be useful for the surface preparation of a wide variety of polymers to be used in cardiovascular and other implantable devices.[14]

Membranes, Blends, and IPN's

Cross-linked **1** or **5** can serve as effective semi-permeable membranes. However, fine-tuning of membrane permeability can be achieved in three ways: (1) By the use of cosubstituent polymers that contain either -$NHCH_3$ or $OCH_2CH_2OCH_2CH_2OCH_3$ side groups, plus a second hydrophobic group such as -OCH_2CF_3 or OC_6H_5. The amount of the hydrophobic cosubstituent allows control over the degree of swelling in aqueous media and the permeability of the membrane to different small molecules. (2) By the formation of polymer alloys (blends) between **1** or **5** and classical organic polymers such as polyvinyl, ester, or amide macromolecules. Membrane transport properties can be controlled by the ratios of the macromolecular components.[15] (3) By the formation of partial or complete cross-linked interpenetrating polymer networks. In principle, this method allows a broader range of compositions to be generated than does method 2.[16]

Gel-Immobilized Enzymes

The radiation-cross-linking of **5** in the presence of enzymes brings about the entrappment of enzyme molecules within a hydrogel matrix.[17] For example, urease has been immobilized in this way. The enzyme retains at least 80% of its activity during multiple, sequential exposures to urea. Uses for this methodology in sensors and bioreactors are being investigated.

Ion-Cross-linked Hydrogels

Finally, in one of the most striking uses of water-soluble polyphosphazenes, it has recently been shown that polymer **2**, which is soluble in aqueous potassium or sodium hydroxide solutions, can be cross-linked to hydrogels by exposure to solutions of di- or trivalent cations, such as Ca^{++} or Al^{++}.[18-20] Technology based on this process has been used to prepare microencapsulated living mammalian cells (such as hybridoma liver cells), proteins, and microorganisms. The hydrogel coating is

permeable to small-molecule nutrients and products of metabolism but is impermeable to antibodies. Several uses for this technology that appear to be promising are under development for artificial organ, biotechnology, and immunological research.

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